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YEAR IN CARDIOLOGY SERIES

STATE-OF-THE-ART PAPER

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CLINICAL RESEARCH

INTERVENTIONAL CARDIOLOGY AND SURGERY

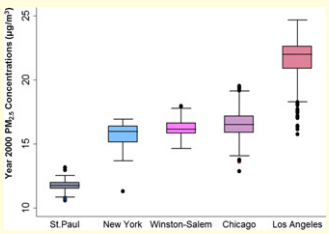
Benefits of CABG Over PCI More Significant in the Elderly **2150**

Marcus Flather, June-Wha Rhee, Derek B. Boothroyd, Eric Boersma, Maria Mori Brooks, Didier Carrié, Tim C. Clayton, Nicholas Danchin, Christian W. Hamm, Whady A. Hueb, Spencer B. King, Stuart J. Pocock, Alfredo E. Rodriguez, Patrick Serruys, Ulrich Sigwart, Rodney H. Stables, Mark A. Hlatky

Flather and colleagues used individual data from 7,812 patients randomized to coronary artery bypass graft (CABG) surgery or percutaneous coronary intervention (PCI) in 10 clinical trials to determine if age modifies the comparative effectiveness of the 2 revascularization procedures. Over a median follow-up of 6 years, the effect of CABG versus PCI on mortality varied according to age, with adjusted CABG:PCI hazard ratios of 1.23 in the youngest tertile, 0.89 in the middle tertile, and 0.79 in the oldest tertile. Further analyses showed that patients over 59 benefitted from CABG, but under 59 there was no difference on mortality.

CARDIOMETABOLIC RISK

Exposure to Fine Particulate Matter Impairs Endothelial Function **2158**



Ranjini M. Krishnan, Sara D. Adar, Adam A. Szpiro, Neal W. Jorgensen, Victor C. Van Hee, R. Graham Barr, Marie S. O'Neill, David M. Herrington, Joseph F. Polak, Joel D. Kaufman

MESA Air (Multi-Ethnic Study of Atherosclerosis and Air Pollution) evaluated the association of long- and short-term air pollutant exposures with flow-mediated dilation (FMD) and brachial arterial diameter (BAD) in a large multi-city cohort. Long-term PM2.5 concentrations were estimated for the year 2000 at each participant residence. Short-term PM2.5 concentrations were based on daily central-site monitoring in each of the six cities. An increase in long-term PM2.5 concentration of 3 $\mu g/m^3$ was associated with a 0.3% decrease in FMD. Women, non-smokers, younger participants, and those with hypertension appeared to show a greater association of PM2.5 with FMD. FMD was not significantly associated with short-term variation in PM2.5. Long-term PM2.5 exposure is associated with decreased endothelial function.

Editorial Comment: Robert D. Brook, Sanjay Rajagopalan, p. 2167

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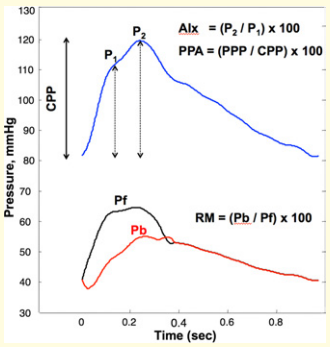
HEART FAILURE



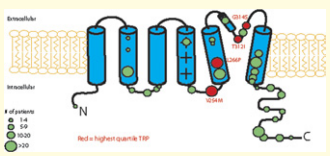
Arterial Wave Reflections and Incident Cardiovascular Events 2170

Julio A. Chirinos, Jan G. Kips, David R. Jacobs Jr, Lyndia Brumback, Daniel A. Duprez, Richard Kronmal, David A. Bluemke, Raymond R. Townsend, Sebastian Vermeersch, Patrick Segers

Experimental and physiologic data mechanistically implicate wave reflections in the pathogenesis of left ventricular failure and cardiovascular disease. Chirinos et. al. derived aortic pressure waveforms from the radial pressure waveforms in nearly 6,000 participants in the MESA (Multiethnic Study of Atherosclerosis). The central pressure waveform was separated into forward and reflected waves using a physiologic flow waveform. Reflection magnitude (RM = [reflected/forward wave amplitude] × 100), augmentation index (Aix = [second/first systolic peak] × 100) and pulse pressure amplification (PPA = [radial/aortic pulse pressure] × 100) were calculated. After adjustment for established risk factors, aortic AIx independently predicted hard cardiovascular events (CVE); PPA independently predicted all CVE. RM was independently predictive of all CVE and strongly predictive of new-onset CHF.

Editorial Comment: Sanjiv J. Shah, J. Andrew Wasserstrom, p. 2178

HEART RHYTHM DISORDERS



In Silico Cardiac Risk Assessment of Long QT Ttype 1 Mutations 2182

Ryan Hoefen, Matthias Reumann, Ilan Goldenberg, Arthur J. Moss, Jin O-Uchi, Yiping Gu, Scott McNitt, Wojciech Zareba, Christian Jons, Jorgen K. Kanters, Pyotr G. Platonov, Wataru Shimizu, Arthur A. M. Wilde, John Jeremy Rice, Coeli M. Lopes

Hoefen and associates studied the ability of a systems level computational model to predict the consequences of complex changes in channel function to the overall heart rhythm and the risk to patients with long QT syndrome (LQTS). A total of 633 LQT1 genotyped subjects with 34 mutations were studied. Cellular electrophysiology function was determined for the mutations and the mutation effect on transmural repolarization was determined for each mutant and related to the risk of cardiac events (syncope, aborted cardiac arrest (ACA), and sudden cardiac death). Multivariate analysis showed that mutation-specific transmural repolarization prologation (TRP) calculated by the model was associated with increased risk of cardiac events (35% per 10 ms increment) independently of the patient's QTc.

Editorial Comment: Ravi Mandapati, Kalyanam Shivkumar, p. 2192

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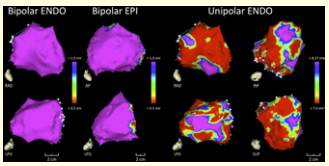

HEART RHYTHM DISORDERS

New Unipolar Electrogram Criteria to Identify Irreversibility of Nonischemic LV Cardiomyopathy **2194**

Bieito Campos, Miguel E. Jauregui, Kyoung-Min Park, Stavros E. Mountantonakis, Edward P. Gerstenfeld, Haris Haqqani, Fermin C. Garcia, Mathew D. Hutchinson, David J. Callans, Sanjay Dixit, David Lin, Michael P. Riley, Wendy Tzou, Joshua M. Cooper, Rupa Bala, Erica Zado, Francis E. Marchlinski

Campos and colleagues report on the utility of left ventricular (LV) endocardial (ENDO) unipolar electroanatomical mapping (EAM) to identify which patients with non-ischemic cardiomyopathy are likely to recover LV systolic function. Detailed ENDO LV EAM was performed in 3 groups: 1) patients with irreversible LV dysfunction but with no or minimal macroscopic scar on MCR imaging; 2) patients with LV dysfunction that reversed after ablation of frequent PVCs; and 3) patients with structurally normal hearts. Areas of unipolar abnormality represented a large proportion of total LV surface in the irreversible group (61%) compared to reversible (8.5%) and normals (1.1%). These results confirm that unipolar voltage mapping can identify irreversible myocardial dysfunction consistent with fibrosis and may serve as valuable prognostic tool.

CARDIAC IMAGING

Prognostic Value of CT Angiography Superior to Exercise Electrocardiogram **2205**

Iksung Cho, Jaemin Shim, Hyuk-Jae Chang, Ji Min Sung, Youngtaek Hong, Hackjoon Shim, Young Jin Kim, Byoung Wook Choi, James K. Min, Ji-Ye Kim, Chi-Young Shim, Geu-Ru Hong, Namsik Chung

Cho and associates sought to determine the prognostic value of multidetector coronary computed tomographic angiography (cCTA) in relation to exercise electrocardiography (XECG). Almost 3,000 patients underwent both cCTA and XECG. Although both XECG (C-statistics: 0.790) and cCTA (0.908) improved risk stratification beyond clinical risk factors, XECG with cCTA did not provide better discrimination than cCTA alone. In subgroup analyses, cCTA stratified risk of MACE both in positive and negative XECG groups; but positive XECG predicted the risk of MACE only in subjects with moderate and severe stenosis by cCTA. These results show that in patients with suspected CAD, cCTA discriminates future risk of MACE independent of XECG results and might, thus, be a better first-line test.

Editorial Comment: Andrew J. Taylor, p. 2216

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BIOMARKERS

Oxidation-Specific Biomarkers Improve Prediction of Cardiovascular and Stroke Outcomes 2218

Sotirios Tsimikas, Peter Willeit, Johann Willeit, Peter Santer, Manuel Mayr, Qingbo Xu, Agnes Mayr, Joseph L. Witztum, Stefan Kiechl

Oxidation-specific epitopes (OSE) are immunogenic, pro-inflammatory and pro-atherogenic and include oxidized phospholipids on apolipoprotein B-100 (OxPL/apoB) and IgG and IgM autoantibodies to malondialdehyde-modified (MDA-LDL) and copper-oxidized low density lipoproteins (Cu-OxLDL). Tsimikas and colleagues studied the long-term predictive value and net reclassification of OSE for the risk of cardiovasular disease (CVD) in a large population based cohort. The highest tertile of OxPL/apoB was associated with higher risk of CVD (hazard ratio [HR]: 2.4) and stroke (HR: 3.6), compared to the lowest tertile. Using OxPL/apoB, IgG Cu-OxLDL and IgM MDA-LDL variables, the area under the curve (AUC) and the net reclassification index both improved substantially. This study demonstrates the clinical value of OSE for predicting the future risk of CVD events.

PERIPHERAL VASCULAR DISEASE

Temporal Trends and Geographic Variation of LE Amputation in Patients With PAD 2230

W. Schuyler Jones, Manesh R. Patel, David Dai, Sumeet Subherwal, Judith Stafford, Sarah Calhoun, Eric D. Peterson

Jones and colleagues used data from the Centers for Medicare & Medicaid Services (CMS) to characterize temporal trends, patient-specific factors, and geographic variation associated with amputation rates in patients with lower extremity peripheral artery disease (LE PAD). In almost 3 million patients with diagnosed PAD, the overall rate of LE amputation declined from 7,258 per 100,000 PAD patients in the year 2000 to 5,790 in 2008. Male sex, black race, diabetes mellitus, and renal disease were all independent predictors of LE amputation, but there was also significant geographic variation that was not easily explained.

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PRE-CLINICAL RESEARCH

PRE-CLINICAL RESEARCH

Kang and colleagues investigated whether cytokine enhancement of a biodegradable patch could restore cardiac function following surgical ventricular restoration (SVR) even when seeded with cells from old donors. Two pro-angiogenic cytokines (vascular endothelial growth factor [VEGF] and basic fibroblast growth factor [bFGF]) were bonded onto porous collagen scaffolds which were then seeded with human mesenchymal stromal cells (hMSCs) from young or old donors. The patches were characterized and used for SVR in a rat model of myocardial infarction. In vitro results showed that cells from old donors grew slower in the scaffolds, but the presence of the cytokines converted the old cell phenotype to a young one. The in vivo studies showed similar beneficial results with cytokine enhancement. This sustained-release, cytokine-conjugated system provides a promising platform for engineering myocardial tissue for aged patients after a myocardial infarction.

Editorial Comment: Emerson C. Perin, James T. Willerson, p. 2250